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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/554,410	11/17/2005	Giovanni Paganelli	725.1049	4581

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EXAMINER
GUSSOW, ANNE

ART UNIT	PAPER NUMBER
1643	

NOTIFICATION DATE	DELIVERY MODE
08/25/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

info@lmiplaw.com

Office Action Summary	Application No.	Applicant(s)	
	10/554,410	PAGANELLI ET AL.	
	Examiner	Art Unit	
	ANNE M. GUSSOW	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 May 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-7,9,11-14 and 18-39* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3-7,9,11-14 and 18-39* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1, 14, 18, 21, 23, 25, and 29 have been amended.

Claims 2, 8, 10, and 15-17 have been cancelled.

Claims 30-39 have been added.

2. Claims 1, 3-7, 9, 11-14, and 18-39 are under examination.

Rejections Maintained

Claim Rejections - 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

4. The rejection of claims 1, 3-7, 9, 11-13, 18-29, and newly added claims 30-39 under 35 U.S.C. 103(a) as being obvious over Goldenberg (US PG PUB 2001/0006618, published July 5, 2001) in view of Cokgor, et al. (Journal of Clinical Oncology, 2000. Vol. 18, pages 3862-3872) is maintained.

Applicant's arguments filed May 29, 2009 have been carefully considered by the examiner but they are deemed not to be persuasive. The response states in part that according to Applicants' present invention and the present set of claims, avidin is

directly administered during the intraoperative locoregional phase, since it is endowed with a certain amount of tumor tropism and therefore concentrates in the therapeutic target sites, followed by systemic administration of radiolabelled biotin or biotin used as a vehicle for anticancer agents, such as, for example, chemotherapeutic agents or toxins or anticancer cells (see page 7-8 of Applicants' specification). Goldenberg does not administer avidin during surgery followed by an anticancer agent with affinity for avidin. Nothing was administered intraoperatively via a locoregional route to the patient. There was also no reason to reverse Goldenberg's order of administering avidin and biotinylated antibody. (see response pages 9-12).

In response to this argument, Goldenberg clearly contemplates the avidin/biotin components to be interchangeable in so far as which is administered first (paragraph 36), thus the method of example 3 could be performed by administering the avidin preparation first followed by the biotinylated preparation. The office action mailed November 26, 2007 clearly set forth that Goldenberg failed to teach administration of a tumor therapy by a locoregional route and that the locoregional administration was taught by Cokgor (page 7 of the office action). The examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, the avidin/biotin therapy of Goldenberg was combined with the

locoregional administration of Cokgor. Both references teach cancer therapy with antibodies. The Cokgor reference teaches reasons for the locoregional administration of therapy being advantageous over systemic administration including reducing the lack of antibody specificity and less than optimal binding affinity, and reducing high interstitial fluid pressure in tumors and surrounding normal tissue (page 3862 2nd column).

Regarding the tumor specificity of avidin, the tumor tropism is an inherent property of the avidin such that administration of avidin would necessarily bind to the tumor whether or not Goldenberg specifically identified the avidin tumor tropism.

Thus, one of ordinary skill in the art would have been motivated to and had a reasonable expectation of success to administer either a first avidin composition or a first biotin composition followed by either a biotin or avidin composition as taught by Goldenberg using the locoregional route of administration as taught by Cokgor.

Therefore after a fresh consideration of the claims and the evidence provided the rejection is maintained.

5. The rejection of claims 1, 3-7, 11-14, 18-29 and newly added claims 30-39 under 35 U.S.C. 103(a) as being obvious over Goldenberg (US PG PUB 2001-0006618, published July 5, 2001) in view of Cokgor, et al. (Journal of Clinical Oncology, 2000. Vol. 18, pages 3862-3872) and MacPhee, et al. (US PAT 6,054,122, issued April 25, 2000) is maintained.

Applicant's arguments filed May 29, 2009 have been carefully considered by the examiner but they are deemed not to be persuasive. The response states that it is

submitted that MacPhee is not relevant to the claimed methods because the newly cited document solves the problem of treating wounded tissue. One of ordinary skill in the art would not have received any guidance from MacPhee and would not have looked to its disclosure when confronted with an invention related to the technical field of tumors and their treatment. MacPhee discloses spray application for external wounds but not for internal application, such as during a surgical procedure (column 25, lines 38-44). In Applicants' claimed method, the agent that can be administered by spray is the first agent which is administered intraoperatively via a locoregional route (see response pages 12-13).

In response to this argument, as set forth above Goldenberg clearly contemplates the avidin/biotin components to be interchangeable in so far as which is administered first (paragraph 36), thus the method of example 3 could be performed by administering the avidin preparation first followed by the biotinylated preparation. The office action mailed November 26, 2007 clearly set forth that Goldenberg failed to teach administration of a tumor therapy by a locoregional route and that the locoregional administration was taught by Cokgor (page 7 of the office action). The examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, the avidin/biotin therapy of Goldenberg

was combined with the locoregional administration of Cokgor. Both references teach cancer therapy with antibodies. The Cokgor reference teaches reasons for the locoregional administration of therapy being advantageous over systemic administration including reducing the lack of antibody specificity and less than optimal binding affinity, and reducing high interstitial fluid pressure in tumors and surrounding normal tissue (page 3862 2nd column).

Regarding the tumor specificity of avidin, the tumor tropism is an inherent property of the avidin such that administration of avidin would necessarily bind to the tumor whether or not Goldenberg specifically identified the avidin tumor tropism.

Regarding the spray application of Mac Phee, the reference explicitly teaches "it can also be applied internally, such as during a surgical procedure" (paragraph 57). In this instance the “it” is a fibrinin sealant which as taught by MacPhee may be supplemented with regulatory compounds, antibodies, antimicrobial compositions, analgesics, anticoagulants ... (see abstract)

Thus, one of ordinary skill in the art would have been motivated to and had a reasonable expectation of success to administer either a first avidin composition or a first biotin composition followed by either a biotin or avidin composition as taught by Goldenberg using the locoregional route of administration as taught by Cokgor with the spray application of MacPhee because MacPhee clearly teaches internal application of the fibrinin sealant comprising other pharmaceutically beneficial compounds.

Therefore after a fresh consideration of the claims and the evidence provided the rejection is maintained.

Conclusion

6. No claims are allowed.

7. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to ANNE M. GUSSOW whose telephone number is (571)272-6047. The examiner can normally be reached on Monday - Friday 8:30 am - 5 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on (571) 272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Anne M. Gussow
August 20, 2009

/Anne M Gussow/
Examiner, Art Unit 1643

/David J Blanchard/
Primary Examiner, Art Unit 1643